UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,015	10/17/2003	Neil H. Bander	10448-196001 /MPI02-192;	3805

26161 7590 04/24/2006

FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
JUEDES, AMY E	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/688,015	BANDER, NEIL H.	
	Examiner	Art Unit	
	Amy E. Juedes, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's species election without traverse, in the reply filed on 3/13/06 is acknowledged. Applicant has elected treating a patient with only an insulin related disorder, the insulin related disorder type 2 diabetes, a method further comprising monitoring insulin dependence, and a method comprising administering a PSMA specific antibody alone. It is noted that the instant claims appear to be free of the art, and thus all the species are under examination.

Claims 1-17 read on the elected invention and are being acted upon.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) set forth below:

The Sequence Listing filed on 10/17/03 is considered non-compliant because it is not properly signed by a registered attorney or agent, see MPEP 714.01(a) which states:

(b) Amendments and other papers. Amendments and other papers, except for written assertions pursuant to § 1.27(c)(2)(ii) of this part, filed in the application must be signed by:

(1) A registered attorney or agent of record appointed in compliance with § 1.34(b);

(2) A registered attorney or agent not of record who acts in a representative capacity under the provisions of § 1.34(a);

(3) An assignee as provided for under § 3.71(b) of this chapter; or

(4) All of the applicants (§ 1.41(b)) for patent, unless there is an assignee of the entire interest and such assignee has taken action in the application in accordance with § 3.71 of this chapter [underlining added by Examiner].

The paper is signed by a Ms. Janice L. Kugler who appears to be none of the above, as evidenced by the absence of a registration number.

3. Applicant's information disclosure, filed 8/2/04, is

acknowledged. However, the ATTC deposit (cite AIIII) has been lined through since it has not been identified by author, title, publisher, and relevant pages, as is required. See MPEP § 609. Additionally, the reference has not been provided.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 1 is indefinite in the recitation of "insulin-related disorder". The specification does not specifically define "insulin-related disorder", but dependent claim 3 gives examples of said disorders, including obesity, hyperglycemia, hypoglycemia, hyperinsulinemia, insulin-resistance, impaired glucose tolerance, impaired fasting glucose, and diabetes (type I, type II and gestational). While diabetes can be considered an insulin-related disorder, hyperglycemia, hypoglycemia, hyperinsulinemia, insulin resistance, impaired glucose tolerance, impaired fasting glucose are symptoms of diabetes, and cannot be considered "insulin-related disorders" as claimed. Additionally, while obesity may be a precipitating factor for diabetes, it is not an "insulin related disorder" as claimed.

B) Claim 2 is indefinite in the recitation of a co-existing "aggravating or precipitating condition". The instant specification does not define the term, and it is unclear exactly what an "aggravating condition" or "precipitating condition" comprises. Thus the metes and bounds of the claims cannot be established.

C) Claim 13 is unclear since it is missing a period and is not a full sentence.

D)Claim 16 recites the limitation "the at least one agent useful in the treatment of diabetes" in line 1-2. There is insufficient antecedent basis for this limitation in the claim. Thus, it is not clear how the agent relates to the claimed method

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 12-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of "cytotoxic agents", "antimetabolic agents", "immunosuppressive" or "immunomodulatory" drugs, or "agents useful in the treatment of an insulin related disorder".

The instant specification does not define the term "cytotoxic agents". Thus, it must be assumed that "cytotoxic agents" represents a broad genus of agents, and includes anything capable of mediating cellular toxicity. This might include structurally different agents, such as antibodies that induce cell death, cytokines, viruses, or even azide or bleach. The instant specification does disclose on pg. 11 several cytotoxic agents such as cyclophosphamide, busulfan, dibromomrmnitol, streptozotocin, mitomycin C, cis-dichlorodiamine platinum, cisplatin, anthracyclines, and anti-mitotic agents. However, this cannot be considered sufficient to represent the broad genus of structurally different "cytotoxic agents" encompassed by the claims.

The instant specification does not define the terms "antimetabolic agents". Thus, it must be assumed that "antimetabolic agents" is the recitation of a broad genus of agents, encompassing any agent that interferes with cellular metabolism. This might encompass chemotherapeutic drugs, antibodies, hormones, etc. In contrast to the broad genus encompassed by "antimetabolic agents", Applicant has not disclosed a single species. Likewise, "immunosuppressive/immunomodulatory" drugs is an extremely large and might encompass any agent that can suppress or modulate the

immune system, such as cytokines, antibodies, cyclosporine, etc. Furthermore, Applicant has not disclosed a single species of "immunosuppressive/immunomodulatory" drugs.

Furthermore, "agents useful in the treatment of an insulin related disorder" represents a broad range of agents. The genus might encompass agents useful for treating any insulin related disorder, for example, type I diabetes, type II diabetes etc. Therefore the claims encompass a broad range of structurally and functionally distinct agents. For example, the claims might encompass T cell depleting antibodies or DNA vaccines that are used for inducing immune tolerance in type I diabetes, or drugs that improve insulin sensitivity. Furthermore, since insulin related disorders encompasses hyperglycemia, the "agents" might include glucose or glucose containing solutions such as soda, that might "treat" hyperglycemia, or even aspirin to treat associated pain. While the instant specification does disclose several examples of agents, such as insulin, sulfonylurea, biguanide, thiazolidinedione, and alpha-glucosidase inhibitor, this is not an adequate disclosure to sufficiently represent the large genus of structurally and functionally different agents encompassed by the claims. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genuses. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

7. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed method could function to treat or prevent an insulin-related disorder, as broadly claimed.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the

quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The method of the instant claims is drawn to treating or preventing insulin related disorders by administering a PSMA specific antibody. It is noted that the instant claims define insulin related disorders as including hyperglycemia, hypoglycemia, impaired glucose tolerance, impaired fasting glucose, obesity, insulin resistance, type I diabetes, type II diabetes, and gestational diabetes. Thus the claims encompass treating or preventing a wide range of different disorders with a PSMA specific antibody. PSMA stands for prostate specific membrane antigen, and is primarily expressed in the prostate (see Holmes, 2001, pg. 511), and increased in prostate cancer. PSMA specific antibodies have been administered to treat prostate cancer, and also to image prostate cancer cells in vivo (see Holmes, 2001, pg. 515-516). It is known that administration of PSMA specific antibodies targets prostate cancer tissue, without localization to other tissues (see Holmes, 2001, pg. 516).

The instant claims are drawn to treating insulin related disorders, such as diabetes. There are two predominant forms of diabetes, Type I and Type 2 diabetes. While both types of diabetes may have similar symptoms, such as hyperglycemia, they

are very different in term of etiology and pathological mechanism. For example, type I diabetes is caused by an immune mediated destruction of pancreatic beta cells, which leads to a deficiency of insulin (see Merck Manual, "Diabetes Mellitus", pg. 1). In contrast, type II diabetes is usually the result of a loss of responsiveness to insulin, and can be precipitated by obesity (see Merck Manual, "Diabetes Mellitus", pg. 1-2). Given the divergent etiologies and pathological mechanisms, it seems unlikely that a single treatment could be effective in treating both type I and type II diabetes, as claimed. Furthermore, PSMA is not known to be involved in the pathogenesis of type I or type II diabetes, and there is no apparent connection in the art that would explain how a prostate specific antibody could be used to treat any type of diabetes. Furthermore, the claims even encompass treating gestational diabetes, which occurs during pregnancy in women who do not even have a prostate. Additionally, it is noted that the claims encompass treating insulin related disorders, including gestational diabetes, by administering a combination of PSMA specific antibody and thalidomide or retinoids. Thalidomide and retinoids are well known to cause birth defects (see Wu et al, pg. 254 and Danzer et al., pg. 468), and would be unsuitable for treating gestational diabetes in pregnant women. In addition to treating diabetes, the instant claims also encompass treating obesity, which typically requires weight loss and exercise. It is unclear how administering a PSMA specific antibody can be expected to treat obesity, as claimed. Furthermore, the instant claims encompass treating symptoms of diabetes, such as hyperglycemia or hypoglycemia. However, both hypoglycemia and hyperglycemia are caused by a wide variety of conditions, in addition to diabetes. For example, hyperglycemia can be caused by obesity or eating disorders, while hypoglycemia can be caused by liver enzyme deficiencies, endotoxic shock, hypopituitarism, or insulinoma, (see Wikipedia, "Hyperglycemia" and Merck Manual "Hypoglycemia"). Thus, it is unclear how the claimed method can be effective for treating hyperglycemia or hypoglycemia caused by such a divergent set of conditions. Additionally, the claims encompass not only treating, but prevention of all insulin related disorders. This would require predicting which patients would be expected to develop insulin disorders, and administering an antibody to prevent symptoms from ever developing.

Given the state of the art, in which there is no known relationship between insulin related disorders and prostate

antigens, the instant specification must provide a sufficient and enabling disclosure, commensurate in scope with the instant claims. However, the only working example provided in the specification demonstrates that a PSMA specific antibody administered to a single patient with type II diabetes and prostate cancer resulted in a reduced dependency of the patient on insulin for a two week period. Given the state of the art, this cannot be considered commensurate in scope with claims drawn to treating insulin related disorders, as broadly claimed. The reduced symptoms of diabetes in a single patient after treatment is anecdotal, is not scientifically significant, and might be due only to pure chance. Applicant needs to provide sufficient data in a larger patient population, compared to control patients, to demonstrate the PSMA specific antibody is actually effective for treating type II diabetes, including in patients without prostate cancer. Furthermore, no examples are provided that demonstrate the ability of PSMA specific antibodies to prevent or treat other insulin related disorders with different pathological mechanisms, such as type I diabetes or obesity. Thus, given the state of the prior art, the lack of working examples, and the breadth of the claims, the instantly claimed method must be considered highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amy E. Juedes, Ph.D.
Patent Examiner
Technology Center 1600
March 29, 2006

4/8/06
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER